Naval Medical Center Portsmouth (NMCP) COVID-19 Literature Report #84: Friday, 07 January 2022

Prepared By: Tracy C. Shields, MSIS, AHIP (Ms.; she/her) <tracy.c.shields2.civ@mail.mil>
Naval Medical Center Portsmouth; Library Services, Reference Medical Librarian

Purpose: These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers. Please reach out with questions, suggestions for future topics, or any other feedback. If this report made a difference or impacted patient care, please let me know!

All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Due to the rapid evolution of the literature, I will not update past reports when new information arises; for retracted papers specific to COVID-19, see the list of retracted papers from Retraction Watch.

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The Big Picture

News in Brief

Welcome to the new year (year 3 of the pandemic), where we have a new variant, new grim milestones, and…

"New CDC guidelines were spurred by worries omicron surge could lead to breakdown in essential services" (WP).

You know things aren't going well when the CDC has to explain itself after backlash to the change in quarantine and isolation guidance (CDC; CDC).

"10 lessons I've learned from the Covid-19 pandemic" (STAT).

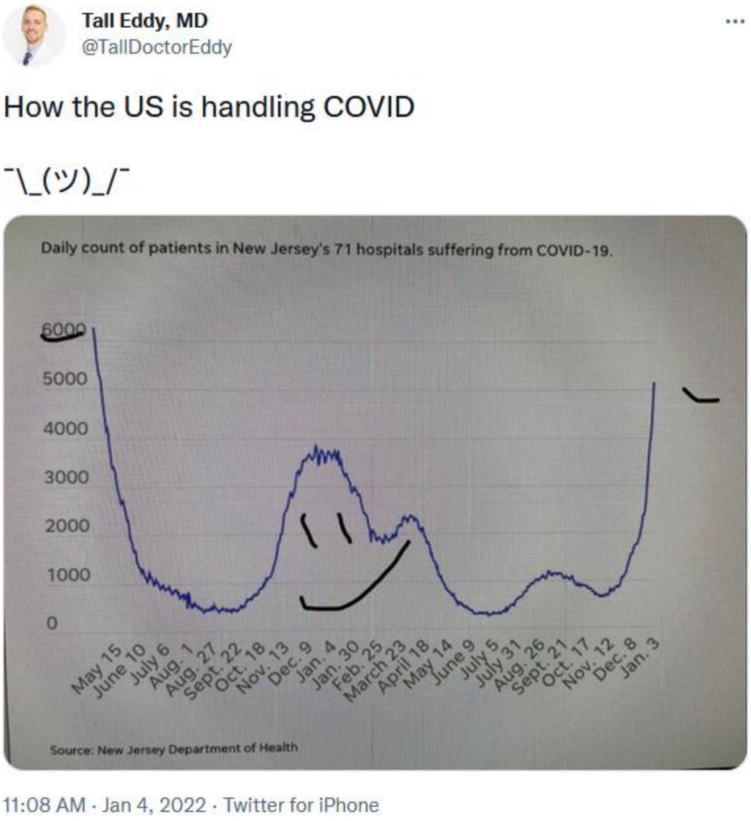
"US hospitals seeing different kind of COVID surge this time" (AP).

"Tales of anguish emerge from China's locked-down Xian, as hospitals demand patients be covid-free" (WP).

"I saw firsthand what it takes to keep COVID out of Hong Kong. It felt like a different planet" (ProPublica).

Listen, It's a Good Joke—It's a Great Joke Even—But I Need You To Stop Anyway

via Twitter:



Tall Eddy, MD
@TallDoctorEddy

How the US is handling COVID

¯_(ツ)_/¯

Daily count of patients in New Jersey's 71 hospitals suffering from COVID-19.

Source: New Jersey Department of Health

11:08 AM · Jan 4, 2022 · Twitter for iPhone

Journal Articles

Lancet Reg Health Am: Minimizing COVID-19 disruption: ensuring the supply of essential health products for health emergencies and routine health services (06 December 2021)

> "Leveraging economies of scale and scope through multi-country pooled procurement enables countries to increase access to quality affordable essential medicines and supplies that meet priority health objectives as well as effectively respond to health emergencies. Strategic partnerships and tools can minimize supply chain disruptions and streamline procurement and deployment in health emergencies, thus mitigating stockouts and ensuring cost efficiencies across various therapeutic areas, including for public health programs at a time when countries may struggle to meet complex needs. As a means to better respond to health emergencies while maintaining priority public health programs, countries should optimize usage of pooled procurement mechanisms facilitated by multilateral technical cooperation and other regional mechanisms, such as the Pan American Health Organization's Strategic Fund. Because few analyses have assessed the role of such regional procurement mechanisms, this Health Policy paper evaluates the key areas of impact of the PAHO Strategic Fund and concludes with lessons learned to help prepare for future health crises while maintaining essential health services."

SARS-CoV-2 Virus and Variants

News in Brief

It looks like a new variant has emerged in Southern France (medRxiv).

"Japan asks US forces to stay on base as COVID-19 cases jump" (AP).

VOC: Omicron

As of 01 January 2022, the omicron variant accounts for 95.4% of cases in the US; it was at 0.6% 4 weeks earlier (CDC Data Tracker).

"How long does omicron take to make you sick?" (Atlantic).

"What we know about the symptoms — and the severity — of the omicron variant" (NPR).

"Omicron is our past pandemic mistakes on fast-forward — we've been making the same errors for nearly two years now" (Atlantic).

"Omicron's feeble attack on the lungs could make it less dangerous — mounting evidence from animal studies suggests that Omicron does not multiply readily in lung tissue, which can be badly damaged in people infected with other variants" (Nature).

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Journal Articles

J Transl Med: Paradoxical sex-specific patterns of autoantibody response to SARS-CoV-2 infection (30 December 2021)

> "Background: Emerging evidence has highlighted the potential importance of autoimmune activation in modulating the acute response and recovery trajectories following SARS-CoV-2 exposure. Given that immune-inflammatory activity can be sex-biased in the setting of severe COVID-19 illness, the aim of the study was to examine sex-specific autoimmune reactivity to SARS-CoV-2 in the absence of extreme clinical disease.
>
> Methods: In this study, we assessed autoantibody (AAB) reactivity to 91 autoantigens previously linked to a range of classic autoimmune diseases in a cohort of 177 participants (65% women, 35% men, mean age of 35) with confirmed evidence of prior SARS-CoV-2 infection based on presence of antibody to the nucleocapsid protein of SARS-CoV-2. Data were compared to 53 pre-pandemic healthy controls (49% women, 51% men). For each participant, socio-demographic data, serological analyses, SARS-CoV-2 infection status and COVID-19 related symptoms were collected by an electronic survey of questions. The symptoms burden score was constructed based on the total number of reported symptoms (N = 21) experienced within 6 months prior to the blood draw, wherein a greater number of symptoms corresponded to a higher score and assigned as more severe burden.
>
> Results: In multivariable analyses, we observed sex-specific patterns of autoreactivity associated with the presence or absence (as well as timing and clustering of symptoms) associated with prior COVID-19 illness. Whereas the overall AAB response was more prominent in women following asymptomatic infection, the breadth and extent of AAB reactivity was more prominent in men following at least mildly symptomatic infection.
>
> Conclusion: Our results reveal that prior SARS-CoV-2 infection, even in the absence of severe clinical disease, can lead to a broad AAB response that exhibits sex-specific patterns of prevalence and antigen selectivity. Further understanding of the nature of triggered AAB activation among men and women exposed to SARS-CoV-2 will be essential for developing effective interventions against immune-mediated sequelae of COVID-19."

Emerg Infect Dis: Epidemiology of COVID-19 after emergence of SARS-CoV-2 Gamma variant, Brazilian Amazon, 2020–2021 (28 December 2021)

> "The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Gamma variant has been hypothesized to cause more severe illness than previous variants, especially in children. Successive SARS-CoV-2 IgG serosurveys in the Brazilian Amazon showed that age-specific attack rates and proportions of symptomatic SARS-CoV-2 infections were similar before and after Gamma variant emergence."

Nature: Broadly neutralizing antibodies overcome SARS-CoV-2 Omicron antigenic shift (23 December 2021)

> "The recently emerged SARS-CoV-2 Omicron variant encodes 37 amino acid substitutions in the spike (S) protein, 15 of which are in the receptor-binding domain (RBD), thereby raising concerns about the effectiveness of available vaccines and antibody therapeutics. Here, we show that the Omicron RBD binds to human ACE2 with enhanced affinity, relative to the Wuhan-Hu-1 RBD, and binds to mouse ACE2. Marked reductions of plasma neutralizing activity were observed against Omicron compared to the ancestral pseudovirus for convalescent and vaccinated individuals, but this loss was less pronounced after a third vaccine dose. Most receptor-binding motif (RBM)-directed monoclonal antibodies (mAbs) lost in vitro neutralizing activity against Omicron, with only 3 out of 29 mAbs retaining unaltered potency, including the ACE2-mimicking S2K146 mAb. Furthermore, a fraction of broadly neutralizing sarbecovirus mAbs neutralized Omicron through recognition of antigenic sites outside the RBM, including sotrovimab, S2X259 and S2H97. The magnitude of Omicron-mediated immune evasion marks a major SARS-CoV-2 antigenic shift. Broadly neutralizing mAbs recognizing RBD epitopes conserved among SARS-CoV-2 variants and other sarbecoviruses may prove key to controlling the ongoing pandemic and future zoonotic spillovers."

Nature: Local and systemic responses to SARS-CoV-2 infection in children and adults (22 December 2021)

> "It is not fully understood why COVID-19 is typically milder in children. To examine differences in response to SARS-CoV-2 infection in children and adults, we analysed paediatric and adult COVID-19 patients and healthy controls (total n=93) using single-cell multi-omic profiling of matched nasal, tracheal, bronchial and blood samples. In healthy paediatric airways, we observed cells already in an interferon-activated state, that upon SARS-CoV-2 infection was further induced especially in airway immune cells. We postulate that higher paediatric innate interferon-responses restrict viral replication and disease progression. The systemic response in children was characterised by increases in naive lymphocytes and a depletion of natural killer cells, while in adults cytotoxic T cells and interferon-stimulated subpopulations were significantly increased. We provide evidence that dendritic cells initiate interferon signaling in early infection, and identify novel epithelial cell states that associate with COVID-19 and age. Our matching nasal and blood data showed a strong interferon response in the airways with the induction of systemic interferon-stimulated populations, which were massively reduced in paediatric patients. Together, we provide several mechanisms that explain the milder clinical syndrome observed in children."

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COVID-19 Vaccines

News in Brief

"Early Israeli findings show fivefold boost from fourth COVID vaccine dose" (CIDRAP).

"FDA shortens interval for booster dose of Moderna COVID-19 vaccine to five months" (FDA).

"US Army creates single vaccine against all COVID & SARS variants, researchers say" (Defense One; see also: Army statement).

"AstraZeneca and Oxford making version of coronavirus vaccine that targets omicron" (WP).

Long Reads

"Amazon delivery — a rainforest expedition brings COVID-19 vaccines to some of Brazil's most remote and vulnerable groups" (Science).

Journal Articles

Vaccines and Variants

NEJM: Effect of Covid-19 Vaccination on Transmission of Alpha and Delta Variants (05 January 2022)

> "Background: Before the emergence of the B.1.617.2 (delta) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), vaccination reduced transmission of SARS-CoV-2 from vaccinated persons who became infected, potentially by reducing viral loads. Although vaccination still lowers the risk of infection, similar viral loads in vaccinated and unvaccinated persons who are infected with the delta variant call into question the degree to which vaccination prevents transmission.
>
> Methods: We used contact-testing data from England to perform a retrospective observational cohort study involving adult contacts of SARS-CoV-2-infected adult index patients. We used multivariable Poisson regression to investigate associations between transmission and the vaccination status of index patients and contacts and to determine how these associations varied with the B.1.1.7 (alpha) and delta variants and time since the second vaccination.
>
> Results: Among 146,243 tested contacts of 108,498 index patients, 54,667 (37%) had positive SARS-CoV-2 polymerase-chain-reaction (PCR) tests. In vaccinated index patients who became infected with the alpha variant, two vaccinations with either BNT162b2 or ChAdOx1 nCoV-19 (also known as AZD1222), as compared with no vaccination, were independently associated with reduced PCR positivity in contacts (adjusted rate ratio with BNT162b2, 0.32; 95% confidence interval [CI], 0.21 to 0.48; and with ChAdOx1 nCoV-19,

> 0.48; 95% CI, 0.30 to 0.78). Vaccine-associated reductions in transmission of the delta variant were smaller than those with the alpha variant, and reductions in transmission of the delta variant after two BNT162b2 vaccinations were greater (adjusted rate ratio for the comparison with no vaccination, 0.50; 95% CI, 0.39 to 0.65) than after two ChAdOx1 vaccinations (adjusted rate ratio, 0.76; 95% CI, 0.70 to 0.82). Variation in cycle-threshold (Ct) values (indicative of viral load) in index patients explained 7 to 23% of vaccine-associated reductions in transmission of the two variants. The reductions in transmission of the delta variant declined over time after the second vaccination, reaching levels that were similar to those in unvaccinated persons by 12 weeks in index patients who had received ChAdOx1 nCoV-19 and attenuating substantially in those who had received BNT162b2. Protection in contacts also declined in the 3-month period after the second vaccination.
>
> Conclusions: Vaccination was associated with a smaller reduction in transmission of the delta variant than of the alpha variant, and the effects of vaccination decreased over time. PCR Ct values at diagnosis of the index patient only partially explained decreased transmission."
>
> Relatedly, see also 3 letters to editor about omicron variant:
>
> - Plasma Neutralization of the SARS-CoV-2 Omicron Variant (30 December 2021)
> - Third BNT162b2 Vaccination Neutralization of SARS-CoV-2 Omicron Infection (29 December 2021)
> - Effectiveness of BNT162b2 Vaccine against Omicron Variant in South Africa (29 December 2021)

Vaccine Hesitancy

Am J Infect Control: Factors and Reasons Associated with Low COVID-19 Vaccine Uptake among Highly Hesitant Communities in the US (04 January 2022)

> "Introduction: The inability to achieve high COVID-19 vaccination rates can continue to have serious harm to our communities. Vaccine hesitancy is a major barrier towards high vaccination rates. We evaluated the relationship between COVID-19 vaccine uptake and vaccine hesitancy, and then examined whether community factors were associated with COVID-19 vaccine uptake and hesitancy.
>
> Methods: We constructed and evaluated a cross-sectional, county-level dataset that included the levels of vaccination uptake and vaccine hesitancy, and population characteristics based on those included in the CDC's Social Vulnerability Index.
>
> Results: Across 3142 US counties, vaccine hesitancy was significantly and negatively correlated with vaccine uptake rates(r=-0.06, p-value<0.01). The two predictors associated

> with a low vaccination level within highly hesitant communities were: no high school education (OR: 0.70, p-value<0.001), and concern on vaccine availability and distribution (CVAC) (OR: 0.00, p-value<0.001). The most common reason driving vaccine hesitancy was lack of trust in COVID-19 vaccines (55%), followed by concerns around side effects of the vaccine (48%), and lack of trust in government (46%).
>
> Conclusion: COVID-19 vaccine hesitancy is a public health threat. Our findings suggests that low education levels are a major contributor to vaccine hesitancy and ultimately vaccination levels. Since education levels are not easily modifiable, our results suggest that policymakers would be best served by closing knowledge gaps to overcome negative perceptions of the vaccine through tailored interventions."

Breakthrough Infections and Reinfections

News in Brief

Secretary of Defense Lloyd J. Austin III, who was fully vaccinated and boostered, tested positive for covid after getting mild symptoms while on leave (DOD).

Long Reads

"I got COVID three times — don't worry, you (probably) won't become me. But yes, you can get COVID twice, and even more" (BuzzFeed).

Journal Articles

MMWR: Risk Factors for Severe COVID-19 Outcomes Among Persons Aged ≥18 Years Who Completed a Primary COVID-19 Vaccination Series — 465 Health Care Facilities, United States, December 2020–October 2021 (07 January 2022)

> "What is already known about this topic? COVID-19 vaccines are highly effective against COVID-19–associated hospitalization and death.
>
> What is added by this report? Among 1,228,664 persons who completed primary vaccination during December 2020–October 2021, severe COVID-19–associated outcomes (0.015%) or death (0.0033%) were rare. Risk factors for severe outcomes included age ≥65 years, immunosuppressed, and six other underlying conditions. All persons with severe outcomes had at least one risk factor; 78% of persons who died had at least four.
>
> What are the implications for public health practice? Vaccinated persons who are older, immunosuppressed, or have other underlying conditions should receive targeted

> interventions including chronic disease management, precautions to reduce exposure, additional primary and booster vaccine doses, and effective pharmaceutical therapy to mitigate risk for severe outcomes. Increasing vaccination coverage is a critical public health priority."

Clin Infect Dis: COVID-19 mRNA vaccines delay the onset of breakthrough infections with less radiographic abnormalities (04 January 2022)

> "This retrospective study of incoming travelers with COVID-19 showed that individuals immunized by mRNA vaccines had significantly longer post-vaccination interval (median: 30.5 days) to breakthrough infection, lower WBC and LDH on admission, and less radiographic abnormalities than those immunized by inactivated virus vaccine who paradoxically had lower respiratory viral load."

Clin Infect Dis: Two cases of breakthrough SARS-CoV-2 infections caused by the Omicron variant (B.1.1.529 lineage) in international travelers to Japan (03 January 2022)

> "In November 2021, the World Health Organization designated a new SARS-CoV-2 variant of concern, Omicron (PANGO lineage B.1.1.529). We report on first two cases of breakthrough COVID-19 caused by Omicron in Japan among international travelers returning from the country with undetected infection. The spread of infection by Omicron were considered."

JAMA Intern Med: Association Between Immune Dysfunction and COVID-19 Breakthrough Infection After SARS-CoV-2 Vaccination in the US (28 December 2021)

> "Question: Is immune dysfunction associated with an increased risk for COVID-19 breakthrough infection after SARS-CoV-2 vaccination?
>
> Findings: In this cohort study of 664 722 patients who received at least 1 dose of a SARS-CoV-2 vaccine, those with immune dysfunction, such as HIV infection, rheumatoid arthritis, and solid organ transplant, had a higher rate for COVID-19 breakthrough infection and worse outcomes after full or partial vaccination, compared with persons without immune dysfunction.
>
> Meaning: The findings suggest that persons with immune dysfunction are at much higher risk for contracting a breakthrough infection and thus should use nonpharmaceutical interventions (eg, mask wearing) and alternative vaccination approaches (eg, additional dose or immunogenicity testing) even after full vaccination."

Treatments and Management

News in Brief

The NIH has updated its COVID-19 treatment guidelines, including information on therapy for use of monoclonal antibodies with omicron variant, potential drug interactions, high-risk, nonhospitalized patients, pre-exposure prophylaxis, and anticoagulation in hospitalized patients (NIH).

Pfizer's Paxlovid (nirmatrelvir and ritonavir co-packaged for oral use) has received EUA for treatment of mild to moderate COVID-19 in adults and children over 12 years old (FDA).

"STAT/Harris Poll: Vaccinated Americans far more likely to take Pfizer Covid-19 pill than unvaccinated people" (STAT).

"The COVID antiviral drugs are here but they're scarce. Here's what to know" (NPR).

"Doctors have an arsenal of Covid-19 treatments, but setbacks and shortages are undercutting options" (STAT).

Journal Articles

Clin Infect Dis: Compassionate Use of REGEN-COV in Patients with COVID-19 and Immunodeficiency-Associated Antibody Disorders (31 December 2021)

> "Background: Patients with immunodeficiency-associated antibody disorders are at a higher risk of prolonged/persistent COVID-19 infection, having no viable treatment options.
>
> Methods: A retrospective analysis of patients with primary and/or secondary immunodeficiency-associated antibody disorders who received casirivimab and imdevimab (REGEN-COV ®) under emergency compassionate use.
>
> Objectives: describe safety and response to REGEN-COV, focusing on the subset of patients who had COVID-19 duration ≥21 days before treatment.
>
> Results: Quantitative (change in oxygenation status and/or viral load) and/or qualitative (physician-reported clinical status) patient outcomes data are reported from 64 patients who received REGEN-COV. Improvement in ≥1 outcome was observed in 90.6% of the overall patient group. Thirty-seven of these had COVID-19 duration ≥21 days before treatment; median time from diagnosis to REGEN-COV was 60.5 days. Of the 29 patients with COVID-19 duration ≥21 days before treatment and available outcome data, 96.6% showed improvement in ≥1 outcome. In the 14 patients with post-treatment RT-PCR results available, 11 (78.6%) reported a negative RT-PCR following treatment, with 5 (45.5%) reporting a negative RT-PCR within 5 days and 8 (72.7%) within 21 days of treatment. Ten of

> 85 patients (11.8%) experienced serious adverse events, only one was an infusion-related reaction, possibly related to REGEN-COV. Two deaths were reported, neither were attributed to REGEN-COV.
>
> Conclusions: In this retrospective analysis of immunodeficient patients granted REGEN-COV under the compassionate use program, REGEN-COV treatment was associated with rapid viral clearance and clinical improvement in patients with long-standing COVID-19. Adverse events were consistent with COVID-19 and its associated complications, and due to patients' concurrent medical conditions."

JAMA Netw Open: Effect of Colchicine vs Usual Care Alone on Intubation and 28-Day Mortality in Patients Hospitalized With COVID-19: A Randomized Clinical Trial (29 December 2021)

> "Question: Does colchicine prevent intubation and mortality in hospitalized patients with COVID-19 pneumonia?
>
> Findings: In this randomized clinical trial of 1279 patients hospitalized with COVID-19, patients allocated to receive colchicine plus usual care or to usual care alone demonstrated no significant difference in the coprimary outcome of mechanical ventilation or 28-day mortality.
>
> Meaning: This randomized clinical trial found that colchicine did not significantly reduce the need for mechanical ventilation or 28-day mortality in patients hospitalized with COVID-19 pneumonia."

NEJM: Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients (22 December 2021)

> "Background: Remdesivir improves clinical outcomes in patients hospitalized with moderate-to-severe coronavirus disease 2019 (Covid-19). Whether the use of remdesivir in symptomatic, nonhospitalized patients with Covid-19 who are at high risk for disease progression prevents hospitalization is uncertain.
>
> Methods: We conducted a randomized, double-blind, placebo-controlled trial involving nonhospitalized patients with Covid-19 who had symptom onset within the previous 7 days and who had at least one risk factor for disease progression (age ≥60 years, obesity, or certain coexisting medical conditions). Patients were randomly assigned to receive intravenous remdesivir (200 mg on day 1 and 100 mg on days 2 and 3) or placebo. The primary efficacy end point was a composite of Covid-19-related hospitalization or death from any cause by day 28. The primary safety end point was any adverse event. A secondary end point was a composite of a Covid-19-related medically attended visit or death from any cause by day 28.

> Results: A total of 562 patients who underwent randomization and received at least one dose of remdesivir or placebo were included in the analyses: 279 patients in the remdesivir group and 283 in the placebo group. The mean age was 50 years, 47.9% of the patients were women, and 41.8% were Hispanic or Latinx. The most common coexisting conditions were diabetes mellitus (61.6%), obesity (55.2%), and hypertension (47.7%). Covid-19-related hospitalization or death from any cause occurred in 2 patients (0.7%) in the remdesivir group and in 15 (5.3%) in the placebo group (hazard ratio, 0.13; 95% confidence interval [CI], 0.03 to 0.59; P = 0.008). A total of 4 of 246 patients (1.6%) in the remdesivir group and 21 of 252 (8.3%) in the placebo group had a Covid-19-related medically attended visit by day 28 (hazard ratio, 0.19; 95% CI, 0.07 to 0.56). No patients had died by day 28. Adverse events occurred in 42.3% of the patients in the remdesivir group and in 46.3% of those in the placebo group.
>
> Conclusions: Among nonhospitalized patients who were at high risk for Covid-19 progression, a 3-day course of remdesivir had an acceptable safety profile and resulted in an 87% lower risk of hospitalization or death than placebo."

NEJM: Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients (16 December 2021)

> "Background: New treatments are needed to reduce the risk of progression of coronavirus disease 2019 (Covid-19). Molnupiravir is an oral, small-molecule antiviral prodrug that is active against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).
>
> Methods: We conducted a phase 3, double-blind, randomized, placebo-controlled trial to evaluate the efficacy and safety of treatment with molnupiravir started within 5 days after the onset of signs or symptoms in nonhospitalized, unvaccinated adults with mild-to-moderate, laboratory-confirmed Covid-19 and at least one risk factor for severe Covid-19 illness. Participants in the trial were randomly assigned to receive 800 mg of molnupiravir or placebo twice daily for 5 days. The primary efficacy end point was the incidence hospitalization or death at day 29; the incidence of adverse events was the primary safety end point. A planned interim analysis was performed when 50% of 1550 participants (target enrollment) had been followed through day 29.
>
> Results: A total of 1433 participants underwent randomization; 716 were assigned to receive molnupiravir and 717 to receive placebo. With the exception of an imbalance in sex, baseline characteristics were similar in the two groups. The superiority of molnupiravir was demonstrated at the interim analysis; the risk of hospitalization for any cause or death through day 29 was lower with molnupiravir (28 of 385 participants [7.3%]) than with placebo (53 of 377 [14.1%]) (difference, -6.8 percentage points; 95% confidence interval, -11.3 to -2.4; P = 0.001). In the analysis of all participants who had undergone randomization, the percentage of participants who were hospitalized or died through day

> 29 was lower in the molnupiravir group than in the placebo group (6.8% [48 of 709] vs. 9.7% [68 of 699]; difference, -3.0 percentage points; 95% confidence interval, -5.9 to -0.1). Results of subgroup analyses were largely consistent with these overall results; in some subgroups, such as patients with evidence of previous SARS-CoV-2 infection, those with low baseline viral load, and those with diabetes, the point estimate for the difference favored placebo. One death was reported in the molnupiravir group and 9 were reported in the placebo group through day 29. Adverse events were reported in 216 of 710 participants (30.4%) in the molnupiravir group and 231 of 701 (33.0%) in the placebo group.
>
> Conclusions: Early treatment with molnupiravir reduced the risk of hospitalization or death in at-risk, unvaccinated adults with Covid-19."

Pre-Existing Conditions and Comorbidities

Journal Articles

JAMA Netw Open: Metabolic Syndrome and Acute Respiratory Distress Syndrome in Hospitalized Patients With COVID-19 (22 December 2021)

> "Question: What is the risk of acute respiratory distress syndrome (ARDS) and death in patients with COVID-19 with metabolic syndrome?
>
> Findings: In this cohort study including 46 441 patients hospitalized for COVID-19, metabolic syndrome was associated with significantly increased odds of ARDS and death. With each metabolic syndrome criterion added from 1 to 4 criteria, the risk of ARDS significantly increased in an additive fashion.
>
> Meaning: These findings suggest that metabolic syndrome and its associated comorbidities were critical risk factors associated with COVID-19–related ARDS and death."

JAMA Intern Med: Comparison of SARS-CoV-2 Antibody Response 4 Weeks After Homologous vs Heterologous Third Vaccine Dose in Kidney Transplant Recipients: A Randomized Clinical Trial (21 December 2021)

> "Question: Does a heterologous SARS-CoV-2 vaccination strategy with the vector vaccine Ad26COVS1 result in a higher rate of antibody response compared with a homologous third dose of mRNA vaccine (mRNA-1273 or BNT162b2) in kidney transplant recipients who did not develop SARS-CoV-2 antibodies after 2 doses of an mRNA vaccine?
>
> Findings: This randomized clinical trial found that a third dose of SARS-CoV-2 vaccine in 197 kidney transplant recipients without antibodies after 2 doses of an mRNA vaccine induced

> an antibody response in 35% of the homologous (mRNA) group vs 42% of the heterologous (vector) group, with no statistically significant difference.
>
> Meaning: The findings of this randomized clinical trial show that homologous and heterologous vaccination strategies for a third SARS-CoV-2 vaccine dose in kidney transplant recipients are comparable, with both mRNA and vector vaccines achieving seroconversion in more than one-third of kidney transplant recipients. However, given the high rate of nonresponders after the third dose, additional strategies to induce an immune response in kidney transplant recipients are urgently needed."

Complications and Coinfections

News in Brief

"What is 'flurona'? Coronavirus and influenza co-infections reported as omicron surges" (WP).

Journal Articles

MMWR: Risk for Newly Diagnosed Diabetes >30 Days After SARS-CoV-2 Infection Among Persons Aged <18 years — United States, March 1, 2020–June 28, 2021 (07 January 2022)

> "What is already known about this topic? SARS-CoV-2 infection is associated with worsening of diabetes symptoms, and persons with diabetes are at increased risk for severe COVID-19. SARS-CoV-2 infection might also induce newly diagnosed diabetes.
>
> What is added by this report? Persons aged <18 years with COVID-19 were more likely to receive a new diabetes diagnosis >30 days after infection than were those without COVID-19 and those with prepandemic acute respiratory infections. Non–SARS-CoV-2 respiratory infection was not associated with an increased risk for diabetes.
>
> What are the implications for public health practice? The increased diabetes risk among persons aged <18 years following COVID-19 highlights the importance of COVID-19 prevention strategies in this age group, including vaccination for all eligible persons and chronic disease prevention and treatment."

J Infect Dis: Lung function decline in relation to COVID-19 in the general population: a matched cohort study with pre-pandemic assessment of lung function (03 January 2022)

> "Objective: To quantify the potential decline in dynamic lung volumes following coronavirus disease 2019 (COVID-19) in the general population.

> Methods: A prospective matched cohort study of adult Copenhagen General Population Study (CGPS) participants with a pre-pandemic spirometry available. CGPS individuals with a positive SARS-CoV-2 polymerase chain reaction (PCR) test performed a repeat spirometry, a questionnaire regarding respiratory symptoms and a diffusing capacity test for carbon monoxide. A matched uninfected CGPS control sample was used, and simple regression and linear mixed effect models were computed to study lung function decline.
>
> Results: A total of 606 were included. 92/107 (85.9%) of individuals with a positive SARS-CoV-2 PCR test experienced COVID-19 symptoms and 12 (11.2%) were hospitalized. Spirometry was performed at a median (interquartile range) of 5.6 (3.9-12.8) months after positive SARS-CoV-2 PCR test. COVID-19 was associated with an adjusted 7.3 mL (95%CI: 0.3-14.3) and 22.6 mL (95%CI: 13.1-32.0) steeper decline in annual FEV1 and FVC or a total of 113.8 and 301.3 ml lower FEV1 and FVC from baseline to follow up. Results were robust in analyses restricted to individuals not requiring hospitalization.
>
> Conclusion: COVID-19 related decline of dynamic lung volumes in the general population not requiring hospitalization were small but measurable."

Brain Res Bull: Risk of ischemic stroke in patients with COVID-19 infection: A Systematic Review and Meta-Analysis (31 December 2021)

> "An ongoing global pandemic, the coronavirus disease 2019 is posing threat to people all over the world. The association between COVID-19 and the risk of ischemic stroke remained unclear. This study systematically reviewed published studies and conducted meta-analysis to evaluate the association between the risk of ischemic stroke and COVID-19. This study was conducted according to guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. The protocol used in this study had been registered in the International Prospective Register of Systematic Reviews. EMBASE, PubMed, Cochrane Library and Web of Science were searched from 1st December 2019 to 19th February 2021. This systematic review and meta-analysis analysed the combined effect estimations based on odds ratios (OR) with the random-effects model. Four studies were screened from 31634 participants including 171 COVID-19 positive patients with ischemic stroke were included. The mean age of COVID-19 positive patients with ischemic stroke was 69.45 years (Range: 63-77 years) and the male patients were 56%. Countries covered by these articles were USA, Italy and France. Three of the articles were retrospective cohort studies and one was prospective cohort study. Our analysis revealed that the risk of ischemic stroke (combined OR: 2.41; 95% CI: 1.08-5.38) was significantly increased. Four included studies were significantly heterogeneous (I2 =75.2%, P = 0.007). Significant association between the risk of ischemic stroke and COVID-19 was observed in the North America group (combined OR: 2.90; 95% CI: 0.45-18.80, I2 = 89.60%, P = 0.002). This study found that the risk for ischemic stroke was increased in COVID-19 patients, especially in patients from North America.

> Further studies with larger sample sizes that include different ethnic populations are required to confirm our analysis."

J Am Heart Assoc: Relationship Between Myocardial Injury During Index Hospitalization for SARS-CoV-2 Infection and Longer-Term Outcomes (31 December 2021)

> "Background: Myocardial injury in patients with COVID-19 is associated with increased mortality during index hospitalization; however, the relationship to long-term sequelae of SARS-CoV-2 is unknown. This study assessed the relationship between myocardial injury (high-sensitivity cardiac troponin T level) during index hospitalization for COVID-19 and longer-term outcomes.
>
> Methods and Results: This is a prospective cohort of patients who were hospitalized at a single center between March and May 2020 with SARS-CoV-2. Cardiac biomarkers were systematically collected. Outcomes were adjudicated and stratified on the basis of myocardial injury. The study cohort includes 483 patients who had high-sensitivity cardiac troponin T data during their index hospitalization. During index hospitalization, 91 (18.8%) died, 70 (14.4%) had thrombotic complications, and 126 (25.6%) had cardiovascular complications. By 12 months, 107 (22.2%) died. During index hospitalization, 301 (62.3%) had cardiac injury (high-sensitivity cardiac troponin T≧14 ng/L); these patients had 28.6%, 32.2%, and 33.2% mortality during index hospitalization, at 6 months, and at 12 months, respectively, compared with 4.1%, 4.9%, and 4.9% mortality for those with low-level positive troponin and 0%, 0%, and 0% for those with undetectable troponin. Of 392 (81.2%) patients who survived the index hospitalization, 94 (24%) had at least 1 readmission within 12 months, of whom 61 (65%) had myocardial injury during the index hospitalization. Of 377 (96%) patients who were alive and had follow-up after the index hospitalization, 211 (56%) patients had a documented, detailed clinical assessment at 6 months. A total of 78 of 211 (37.0%) had ongoing COVID-19-related symptoms; 34 of 211 (16.1%) had neurocognitive decline, 8 of 211 (3.8%) had increased supplemental oxygen requirements, and 42 of 211 (19.9%) had worsening functional status.
>
> Conclusions: Myocardial injury during index hospitalization for COVID-19 was associated with increased mortality and may predict who are more likely to have postacute sequelae of COVID-19. Among patients who survived their index hospitalization, the incremental mortality through 12 months was low, even among troponin-positive patients."

J Fungi: A Visual and Comprehensive Review on COVID-19-Associated Pulmonary Aspergillosis (CAPA) (11 December 2021)

> "Coronavirus disease 19 (COVID-19)-associated pulmonary aspergillosis (CAPA) is a severe fungal infection complicating critically ill COVID-19 patients. Numerous retrospective and prospective studies have been performed to get a better grasp on this lethal co-infection. We performed a qualitative review and summarized data from 48 studies in which 7047

> patients had been included, of whom 820 had CAPA. The pooled incidence of proven, probable or putative CAPA was 15.1% among 2953 ICU-admitted COVID-19 patients included in 18 prospective studies. Incidences showed great variability due to multiple factors such as discrepancies in the rate and depth of the fungal work-up. The pathophysiology and risk factors for CAPA are ill-defined, but therapy with corticosteroids and anti-interleukin-6 therapy potentially confer the biggest risk. Sampling for mycological work-up using bronchoscopy is the cornerstone for diagnosis, as imaging is often aspecific. CAPA is associated with an increased mortality, but we do not have conclusive data whether therapy contributes to an increased survival in these patients. We conclude our review with a comparison between influenza-associated pulmonary aspergillosis (IAPA) and CAPA."

Long COVID / Post-COVID Syndrome

News in Brief

The UK-based Royal College of Occupational Therapists has put out quick guides covering long covid in adults and children (RCOT).

Why that organization is putting the information out there: about 1.3 million people living in the UK -- 2% of the population -- report having long-COVID symptoms (UK gov).

Podcast (20 mins): "How Do We Treat Long COVID?" (Medpage)

Journal Articles

JAMA Otolaryngol Head Neck Surg: Comprehensive Chemosensory Psychophysical Evaluation of Self-reported Gustatory Dysfunction in Patients With Long-term COVID-19: A Cross-sectional Study (06 January 2022)

> "This cross-sectional study evaluates self-reported gustatory dysfunction in patients with long-term COVID-19….
>
> It is widely believed that self-reported loss of taste can be an indirect consequence of retronasal olfactory dysfunction; indeed, our study found that even when specifically asked about basic tastes, more than half of patients self-reporting an altered taste perception exhibited a normal gustatory function, while most of them had an olfactory impairment. However, 42% were found to have true hypogeusia. Following evaluation of the scores in relation to age, still 29% exhibited hypogeusia, which has largely been overlooked to date. While olfactory training may help the former group, additional strategies may be needed for those with gustatory impairment."

Brain Behav Immun: Fatigue and Cognitive Impairment in Post-COVID-19 Syndrome: A Systematic Review and Meta-Analysis (29 December 2021)

> "Objective: To quantify the proportion of individuals experiencing fatigue and cognitive impairment 12 or more weeks following COVID-19 diagnosis, and to characterize the inflammatory correlates and functional consequences of post-COVID-19 syndrome.
>
> Data sources: Systematic searches were conducted without language restrictions from database inception to June 8, 2021 on PubMed/MEDLINE, The Cochrane Library, PsycInfo, Embase, Web of Science, Google/Google Scholar, and select reference lists.
>
> Study selection: Primary research articles which evaluated individuals at least 12 weeks after confirmed COVID-19 diagnosis and specifically reported on fatigue, cognitive impairment, inflammatory parameters, and/or functional outcomes were selected.
>
> Data extraction & synthesis: Two reviewers independently extracted published summary data and assessed methodological quality and risk of bias. A meta-analysis of proportions was conducted to pool Freeman-Turkey double arcsine transformed proportions using the random-effects restricted maximum-likelihood model.
>
> Main outcomes & measures: The co-primary outcomes were the proportions of individuals reporting fatigue and cognitive impairment, respectively, 12 or more weeks after COVID-19 infection. The secondary outcomes were inflammatory correlates and functional consequences of post-COVID-19 syndrome.
>
> Results: The literature search yielded 10,979 studies, and 81 studies were selected for inclusion. The fatigue meta-analysis comprised 68 studies, the cognitive impairment meta-analysis comprised 43 studies, and 48 studies were included in the narrative synthesis. Meta-analysis revealed that the proportion of individuals experiencing fatigue 12 or more weeks following COVID-19 diagnosis was 0.32 (95% CI, 0.27, 0.37; $p < 0.001$; $n = 25,268$; $I2=99.1\%$). The proportion of individuals exhibiting cognitive impairment was 0.22 (95% CI, 0.17, 0.28; $p < 0.001$; $n = 13,232$; $I2=98.0$). Moreover, narrative synthesis revealed elevations in proinflammatory markers and considerable functional impairment in a subset of individuals.
>
> Conclusions & relevance: A significant proportion of individuals experience persistent fatigue and/or cognitive impairment following resolution of acute COVID-19. The frequency and debilitating nature of the foregoing symptoms provides the impetus to characterize the underlying neurobiological substrates and how to best treat these phenomena."

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Ann Neurol: Multisystem Involvement in Post-acute Sequelae of COVID-19 (PASC) (24 December 2021)

> "Objective: To describe cerebrovascular, neuropathic and autonomic features of post-acute sequelae of COVID-19 (PASC).
>
> Methods: This retrospective study evaluated consecutive patients with chronic fatigue, brain fog and orthostatic intolerance consistent with PASC. Controls included postural tachycardia syndrome patients (POTS) and healthy participants. Analyzed data included surveys and autonomic (Valsalva maneuver, deep breathing, sudomotor and tilt tests), cerebrovascular (cerebral blood flow velocity (CBFv) monitoring in middle cerebral artery), respiratory (capnography monitoring) and neuropathic (skin biopsies for assessment of small fiber neuropathy) testing and inflammatory/autoimmune markers.
>
> Results: Nine PASC patients were evaluated 0.7±0.3 years after a mild COVID-19 infection, treated as home observations. Autonomic, pain, brain fog, fatigue and dyspnea surveys were abnormal in PASC and POTS (n=10), compared to controls (n=15). Tilt table test reproduced the majority of PASC symptoms. Orthostatic CBFv declined in PASC (-20.0±13.4%) and POTS (-20.3±15.1%), compared to controls (-3.0±7.5%,p=0.001) and was independent of end-tidal carbon dioxide in PASC, but caused by hyperventilation in POTS. Reduced orthostatic CBFv in PASC included both subjects without (n=6) and with (n=3) orthostatic tachycardia. Dysautonomia was frequent (100% in both PASC and POTS) but was milder in PASC (p=0.013). PASC and POTS cohorts diverged in frequency of small fiber neuropathy (89% vs. 60%) but not in inflammatory markers (67% vs. 70%). Supine and orthostatic hypocapnia was observed in PASC.
>
> Interpretation: PASC following mild COVID-19 infection is associated with multisystem involvement including: 1) cerebrovascular dysregulation with persistent cerebral arteriolar vasoconstriction; 2) small fiber neuropathy and related dysautonomia; 3) respiratory dysregulation; 4) chronic inflammation."

Maternal Health, Pregnancy, and Perinatal Period

Journal Articles

MMWR: Receipt of COVID-19 Vaccine During Pregnancy and Preterm or Small-for-Gestational-Age at Birth — Eight Integrated Health Care Organizations, United States, December 15, 2020–July 22, 2021 (04 January 2022)

> "What is already known about this topic? Pregnant women with COVID-19 are at increased risk for severe illness and adverse birth outcomes, yet many remain reluctant to be vaccinated.
>
> What is added by this report? In a retrospective cohort of >40,000 pregnant women, COVID-19 vaccination during pregnancy was not associated with preterm birth or small-for-gestational-age at birth overall, stratified by trimester of vaccination, or number of vaccine doses received during pregnancy, compared with unvaccinated pregnant women.
>
> What are the implications for public health practice? These data support the safety of COVID-19 vaccination during pregnancy. CDC recommends COVID-19 vaccination for women who are pregnant, recently pregnant, who are trying to become pregnant now, or who might become pregnant in the future."

Pediatrics: [Human Milk SARS-CoV-2 Antibodies up to 6 Months After Vaccination]() (03 January 2022)

> "Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-specific antibodies have been detected in human milk up to 6 weeks post-coronavirus disease 2019 (COVID-19) vaccination. We evaluated SARS-CoV-2-specific antibodies, neutralization activity, effect of pasteurization, and persistence through 6 months after vaccination.
>
> Methods: This prospective longitudinal study enrolled 30 pregnant or lactating women. SARS-CoV-2 antibodies and neutralization capacity were analyzed using an enzyme-linked immunosorbent assay compared at prevaccination and 1, 3, and 6 months postvaccination, and through Holder pasteurization.
>
> Results: Human milk SARS-CoV-2-specific IgG levels peaked at 1 month postvaccination and persisted above prevaccination levels for at least 6 months ($P = .005$). SARS-CoV-2-specific IgA was detected at 1 and 3 months (both $P < .001$) but waned by 6 months compared with baseline ($P = .07$). Milk SARS-CoV-2-specific IgG and IgA correlated with serum IgG at the same time point ($R2 = 0.37$, $P < .001$ and $R2 = 0.19$, $P < .001$). Neutralization activity was seen in 83.3%, 70.4%, and 25.0% of milk samples at 1, 3, and 6 months postvaccination. Neutralization most strongly correlated with SARS-CoV-2-specific IgG ($R2 = 0.57$, $P < .001$). Pre- and postpasteurization samples showed similar IgG (0.84 vs 1.07, $P = .36$) and neutralizing activity (57.7% vs 58.7% inhibition, $P = .27$), but lower IgM and IgA levels postpasteurization (0.09 vs 0.06, $P = .004$ and 0.21 vs 0.18, $P = .043$).
>
> Conclusions: The data suggest that human milk SARS-CoV-2-specific antibodies may be available to milk-fed infants for up to 6 months. In addition, donor milk from vaccinated mothers retain IgG and neutralizing activity."

J Infect Dis: [SARS-CoV-2 infection during pregnancy and associated perinatal health outcomes: a national US cohort study]() (27 December 2021)

> "Background: SARS-CoV-2 infection has been associated with increased risk of adverse perinatal health outcomes. However, few large-scale, community-based epidemiological studies have been conducted.
>
> Methods: We conducted a national cohort study using de-identified administrative claims data for 78,283 pregnancies with estimated conception before 30 April 2020 and pregnancy end after 11 March 2020. We identified maternal infections using diagnostic and laboratory testing data. We compared the risk of pregnancy outcomes using Cox proportional hazard models treating COVID-19 as a time-varying exposure and adjusting for baseline covariates.
>
> Results: 2,655 (3.4%) pregnancies had a documented SARS-CoV-2 infection; 3.4% required admission to intensive care, invasive mechanical ventilation or ECMO treatment. COVID-19 during pregnancy was not associated with risk of miscarriage, antepartum hemorrhage, or stillbirth, but was associated with 2-3 fold higher risk of induced abortion (adjusted hazard ratio [aHR] 2.60, 95% CI 1.17-5.78), c-section (aHR 1.99, 95% CI 1.71-2.31), clinician-initiated preterm birth (2.88; 95% CI 1.93, 4.30), spontaneous preterm birth (aHR 1.79, 95% CI 1.37-2.34), fetal growth restriction (aHR 2.04, 95% CI 1.72-2.43), and postpartum hemorrhage (aHR 2.03, 95% CI 1.6-2.63).
>
> Conclusions: Prenatal SARS-CoV-2 infection was associated with increased risk of adverse pregnancy outcomes. Prevention could have fetal health benefits."

JAMA Pediatr: Maternal and Neonatal SARS-CoV-2 Immunoglobulin G Antibody Levels at Delivery After Receipt of the BNT162b2 Messenger RNA COVID-19 Vaccine During the Second Trimester of Pregnancy (21 December 2021)

> "Question: What were the maternal and neonatal SARS-CoV-2 immunoglobulin G antibody levels at birth after messenger RNA (mRNA) COVID-19 vaccination during the second trimester of pregnancy?
>
> Findings: In this cohort study of 130 pregnant women who received the BNT162b2 mRNA vaccine during their second trimester, antibody titers were positive for all women during delivery, and neonatal titers were higher than maternal titers, representing 100% placental antibody transfer.
>
> Meaning: The findings suggest that administration of the mRNA COVID-19 vaccine during the second trimester is associated with a maternal humoral response that is sustained during labor and transfers antibodies to the neonate, supporting early vaccination of pregnant women."

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Pediatric Population

News in Brief

Under its EUA, the FDA now allows a single booster dose in children 12 through 15 years of age with a shortened booster time of 5 months and a third primary series dose for certain immunocompromised children 5 through 11 years of age (FDA).

"Child Covid hospitalizations are up, especially in 5 states" (NBC).

"Pfizer expects updated COVID-19 vaccine data for kids under 5 by April" (Reuters).

"Schools use therapy-based programs for 'overwhelmed' kids" (AP).

Journal Articles

JAMA Pediatr: Association of Birth During the COVID-19 Pandemic With Neurodevelopmental Status at 6 Months in Infants With and Without In Utero Exposure to Maternal SARS-CoV-2 Infection (04 January 2022)

> "Question: Is maternal SARS-CoV-2 infection during pregnancy associated with infant neurobehavioral development at age 6 months?
>
> Findings: In this cohort study of 255 infants born between March and December 2020, exposure to maternal SARS-CoV-2 infection was not associated with differences on any Ages & Stages Questionnaire, 3rd Edition, subdomain at age 6 months, regardless of infection timing or severity. However, both exposed and unexposed infants born during that period had significantly lower scores on gross motor, fine motor, and personal-social subdomains compared with a historical cohort of infants born before the onset of the COVID-19 pandemic.
>
> Meaning: These findings suggest that birth during the COVID-19 pandemic, but not maternal SARS-CoV-2 infection, is associated with differences in neurodevelopment at age 6 months."

MMWR: Characteristics and Clinical Outcomes of Children and Adolescents Aged <18 Years Hospitalized with COVID-19 — Six Hospitals, United States, July–August 2021 (31 December 2021)

> "What is already known about this topic? Pediatric COVID-19–related hospitalization rates increased when the highly transmissible SARS-CoV-2 B.1.617.2 (Delta) variant became the predominant circulating strain.
>
> What is added by this report? Among children and adolescents with SARS-CoV-2 infection admitted to six hospitals during July–August 2021, 77.9% were hospitalized for acute

COVID-19. Among these patients, approximately one third aged <5 years had a viral coinfection (approximately two thirds of which were respiratory syncytial virus) and approximately two thirds of those aged 12–17 years had obesity; only 0.4% of age-eligible patients were fully vaccinated.

What are the implications for public health practice? COVID-19 vaccination and other prevention strategies are important to protect children from COVID-19, particularly children with obesity and other underlying health conditions."

Pediatrics: Suicide Risk in Adolescents During the COVID-19 Pandemic (31 December 2021)

"Background: The coronavirus disease 2019 (COVID-19) pandemic created high levels of psychological distress and may have increased suicide risk.

Methods: We used the 4-item Ask Suicide-Screening Questions (ASQ) to assess suicide risk among all patients 12 to 24 years of age at a children's hospital. We compared demographics, encounter type (telehealth or face-to-face [F2F]), and screening results from April to June 2020 (T2) to those from April to June 2019 (T1).

Results: Fewer patients were seen at T2 than T1 (17 986 vs 24 863). A greater proportion of visits at T2 were by telehealth (0% vs 43%). The rate of positive suicide screens was higher in T2 than in T1 (12.2% vs 11.1%, adjusted odds ration [aOR], 1.24; 95% confidence interval [CI], 1.15-1.35). The odds of a positive screen were greater for older patients (aOR of 1.12 for age in years; 95% CI, 1.10-1.14), female patients (aOR, 2.23; 95% CI, 2.00-2.48), patients with public versus private insurance (aOR, 1.88; 95% CI, 1.72-2.07), and lower for Black versus White patients (aOR, 0.85; 95% CI, 0.77-0.95). Rates of positive screens were highest among inpatients (20.0%), intermediate for emergency department patients (14.4%), and lowest in outpatient clinics (9.9%) (P < .05).

Conclusions: Rates of positive suicide risk screens among adolescents rose in the pandemic's early months with differences related to sociodemographics and visit type. Changes in health care delivery highlight the complexities of assessing and responding to mental health needs of adolescents. Additional research might determine the effects of screening methods and patient populations on screening results."

JAMA Netw Open: Factors Associated With Severe Gastrointestinal Diagnoses in Children With SARS-CoV-2 Infection or Multisystem Inflammatory Syndrome (20 December 2021)

"Question: Is COVID-19 associated with severe gastrointestinal manifestations in children?

Findings: In this multicenter cohort study of 685 Italian children with COVID-19, 10% showed severe gastrointestinal involvement characterized by diffuse adeno-mesenteritis, appendicitis, abdominal fluid collection, ileal intussusception, or pancreatitis. Children older than 5 years and those presenting with abdominal pain, leukopenia, or receiving a diagnosis

> of multisystem inflammatory syndrome were more likely to have severe gastrointestinal manifestations.
>
> Meaning: Severe gastrointestinal involvement is not uncommon in children with COVID-19, and awareness about its frequency and presentation may help practitioners to appropriately manage children at risk of severe outcomes."

Nat Med: Risk factors for PICU admission and death among children and young people hospitalized with COVID-19 and PIMS-TS in England during the first pandemic year (20 December 2021)

> "Identifying which children and young people (CYP) are most vulnerable to serious infection due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is important to guide protective interventions. To address this question, we used data for all hospitalizations in England among 0-17 year olds from 1 February 2019 to 31 January 2021. We examined how sociodemographic factors and comorbidities might be risk factors for pediatric intensive care unit (PICU) admission among hospitalizations due to the following causes: Coronavirus Disease 2019 (COVID-19) and pediatric inflammatory multi-system syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in the first pandemic year (2020-2021); hospitalizations due to all other non-traumatic causes in 2020-2021; hospitalizations due to all non-traumatic causes in 2019-2020; and hospitalizations due to influenza in 2019-2020. Risk of PICU admission and death from COVID-19 or PIMS-TS in CYP was very low. We identified 6,338 hospitalizations with COVID-19, of which 259 were admitted to a PICU and eight CYP died. We identified 712 hospitalizations with PIMS-TS, of which 312 were admitted to a PICU and fewer than five CYP died. Hospitalizations with COVID-19 and PIMS-TS were more common among males, older CYP, those from socioeconomically deprived neighborhoods and those who were of non-White ethnicity (Black, Asian, Mixed or Other). The odds of PICU admission were increased in CYP younger than 1 month old and decreased among 15-17 year olds compared to 1-4 year olds with COVID-19; increased in older CYP and females with PIMS-TS; and increased for Black compared to White ethnicity in patients with COVID-19 and PIMS-TS. Odds of PICU admission in COVID-19 were increased for CYP with comorbidities and highest for CYP with multiple medical problems. Increases in odds of PICU admission associated with different comorbidities in COVID-19 showed a similar pattern to other causes of hospitalization examined and, thus, likely reflect background vulnerabilities. These findings identify distinct risk factors associated with PICU admission among CYP with COVID-19 or PIMS-TS that might aid treatment and prevention strategies."

Emerg Infect Dis: Effects of Nonpharmaceutical COVID-19 Interventions on Pediatric Hospitalizations for Other Respiratory Virus Infections, Hong Kong (online 15 November 2021)

> "To determine the effects of nonpharmaceutical interventions (NPIs) for coronavirus disease on pediatric hospitalizations for infection with respiratory viruses other than severe

> acute respiratory syndrome coronavirus 2, we analyzed hospital data for 2017–2021. Compared with 2017–2019, age-specific hospitalization rates associated with respiratory viruses greatly decreased in 2020, when NPIs were in place. Also when NPIs were in place, rates of hospitalization decreased among children of all ages for infection with influenza A and B viruses, respiratory syncytial virus, adenovirus, parainfluenza viruses, human metapneumovirus, and rhinovirus/enterovirus. Regression models adjusted for age and seasonality indicated that hospitalization rates for acute febrile illness/respiratory symptoms of any cause were reduced by 76% and by 85%–99% for hospitalization for infection with these viruses. NPIs in Hong Kong were clearly associated with reduced pediatric hospitalizations for respiratory viruses; implementing NPIs and reopening schools were associated with only a small increase in hospitalizations for rhinovirus/enterovirus infections."

Vaccines

MMWR: Effectiveness of BNT162b2 (Pfizer-BioNTech) mRNA Vaccination Against Multisystem Inflammatory Syndrome in Children Among Persons Aged 12–18 Years — United States, July–December 2021 (07 January 2022)

> "What is already known about this topic? The Pfizer-BioNTech vaccine, currently authorized for persons aged ≥5 years, provides a high level of protection against severe COVID-19 in persons aged 12–18 years. Vaccine effectiveness against multisystem inflammatory syndrome in children (MIS-C), which can occur 2–6 weeks after SARS-CoV-2 infection, has remained uncharacterized.
>
> What is added by this report? Estimated effectiveness of 2 doses of Pfizer-BioNTech vaccine against MIS-C was 91% (95% CI = 78%–97%). Among critically ill MIS-C case-patients requiring life support, all were unvaccinated.
>
> What are the implications for public health practice? Receipt of 2 doses of Pfizer-BioNTech vaccine is highly effective in preventing MIS-C in persons aged 12–18 years. These findings further reinforce the COVID-19 vaccination recommendation for eligible children."

MMWR: Interim Estimate of Vaccine Effectiveness of BNT162b2 (Pfizer-BioNTech) Vaccine in Preventing SARS-CoV-2 Infection Among Adolescents Aged 12–17 Years — Arizona, July–December 2021 (31 December 2021)

> "What is already known about this topic? The Pfizer-BioNTech COVID-19 vaccine has been shown to be effective in preventing SARS-CoV-2 infection in adolescents in randomized placebo-controlled Phase III trials.

> What is added by this report? A prospective cohort of 243 adolescents aged 12–17 years in Arizona completed weekly SARS-CoV-2 testing by nasal swab for 19 consecutive weeks. Under real-world conditions, vaccine effectiveness of full immunization (completion of the second in a 2-dose series ≥14 days earlier) was 92% against SARS-CoV-2 infections irrespective of symptom status.
>
> What are the implications for public health practice? In real-world conditions among adolescents aged 12–17 years, the Pfizer-BioNTech vaccine was highly effective in preventing SARS-CoV-2 infection."

MMWR: COVID-19 Vaccine Safety in Children Aged 5–11 Years — United States, November 3–December 19, 2021 (31 December 2021)

> "What is already known about this topic? In preauthorization trials for Pfizer-BioNTech (BNT162b2) COVID-19 vaccine, vaccinated children aged 5–11 years reported mild to moderately severe local and systemic reactions; no serious vaccination-related events were noted.
>
> What is added by this report? After authorization of Pfizer-BioNTech COVID-19 vaccine for children aged 5–11 years during October 2021, and administration of approximately 8 million doses, local and systemic reactions after vaccination were commonly reported to VAERS and v-safe for vaccinated children aged 5–11 years. Serious adverse events were rarely reported.
>
> What are the implications for public health practice? Parents and guardians of children aged 5–11 years should be advised that local and systemic reactions are expected after vaccination with Pfizer-BioNTech COVID-19 vaccine and are more common after the second dose."

Healthcare Workers

News in Brief

"ICU teams report fatigue and frustration as they brace for omicron surge" (NPR).

Long Reads

"Omicron isn't mild for the health-care system — the new variant is spreading quickly enough to inundate hospitals that were already buckling under the cumulative toll of every previous surge" (Atlantic).

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Journal Articles

BMC Psychiatry: The new frontline: exploring the links between moral distress, moral resilience and mental health in healthcare workers during the COVID-19 pandemic (06 January 2022)

> "Background: Global health crises, such as the COVID-19 pandemic, confront healthcare workers (HCW) with increased exposure to potentially morally distressing events. The pandemic has provided an opportunity to explore the links between moral distress, moral resilience, and emergence of mental health symptoms in HCWs.
>
> Methods: A total of 962 Canadian healthcare workers (88.4% female, 44.6 + 12.8 years old) completed an online survey during the first COVID-19 wave in Canada (between April 3rd and September 3rd, 2020). Respondents completed a series of validated scales assessing moral distress, perceived stress, anxiety, and depression symptoms, and moral resilience. Respondents were grouped based on exposure to patients who tested positive for COVID-19. In addition to descriptive statistics and analyses of covariance, multiple linear regression was used to evaluate if moral resilience moderates the association between exposure to morally distressing events and moral distress. Factors associated with moral resilience were also assessed.
>
> Findings: Respondents working with patients with COVID-19 showed significantly more severe moral distress, anxiety, and depression symptoms ($F > 5.5$, $p < .020$), and a higher proportion screened positive for mental disorders (Chi-squared > 9.1, $p = .002$), compared to healthcare workers who were not. Moral resilience moderated the relationship between exposure to potentially morally distressing events and moral distress ($p < .001$); compared to those with higher moral resilience, the subgroup with the lowest moral resilience had a steeper cross-sectional worsening in moral distress as the frequency of potentially morally distressing events increased. Moral resilience also correlated with lower stress, anxiety, and depression symptoms ($r > .27$, $p < .001$). Factors independently associated with stronger moral resilience included: being male, older age, no mental disorder diagnosis, sleeping more, and higher support from employers and colleagues (B [0.02, |-0.26|].
>
> Interpretation: Elevated moral distress and mental health symptoms in healthcare workers facing a global crisis such as the COVID-19 pandemic call for the development of interventions promoting moral resilience as a protective measure against moral adversities."

J Infect Dis: Effect of influenza vaccination on risk of COVID-19 – A prospective cohort study of 46,000 health care workers (05 January 2022)

> "The purpose of this study was to assess if influenza vaccination has an impact on the risk of COVID-19. A cohort of 46,112 health care workers were tested for antibodies against SARS-CoV-2 and filled in a survey on COVID-19 symptoms, hospitalization, and influenza

> vaccination. The RR of hospitalization due to SARS-CoV-2 for influenza vaccinated compared with unvaccinated participants was 1.00 for the seasonal vaccination in 2019/2020 (CI 0.56-1.78, p=1.00). Likewise, no clinical effect of influenza vaccination on development of antibodies against SARS-CoV-2 was found. The present findings indicate that influenza vaccination does not affect the risk of SARS-CoV-2 infection or COVID-19."

Infect Dis: An episode of transmission of COVID-19 from a vaccinated healthcare worker to co-workers (14 December 2021)

> "Background: Reports of transmission of COVID-19 from a vaccinated healthcare worker (HCW) to vaccinated co-workers are sparse.
>
> Methods: Index case (IC): After the second dose of the ChAdOx1 nCoV-19 vaccine, a HCW – our IC was diagnosed of COVID-19 by a rapid antigen test (RAT). A reverse transcription-polymerase chain reaction (RT-PCR) test done on the same day showed a cycle threshold (Ct) value of 10.02 (a very high viral load). Contact tracing and findings: The authors traced IC's contacts and seven contacts were identified. Four of those (P 1–4) were tested positive for COVID-19 on day12 after the contact. P1–2 were vaccinated and had slept near the IC in an enclosed 5.5 × 2.7 × 2.4 m room without air change and without masks, while IC was symptomatic. P3 and P4 came in immediately after IC left that room and slept there without masks. We did not find any other exposures of P1–4 within the 14 days (d) before they tested positive.
>
> Conclusions: P1 and P2 are COVID-19 vaccine breakthrough infections. P3 and P4 contracting infection in the physical absence of IC indicates probable aerosol transmission of COVID-19. The factors that led to this episode, namely, unfamiliarity of breakthrough COVID-19 infections, ignoring the risk of contracting COVID-19 from vaccinated co-workers, hesitancy in seeking medical care soon after the onset of symptoms, poorly ventilated and cramped resting rooms for HCW exists worldwide. This episode reiterates the importance of adhering to basic COVID-19 preventive measures even after vaccination."

Emerg Infect Dis: Risk Factors for SARS-CoV-2 Infection Among US Healthcare Personnel, May–December 2020 (02 December 2021)

> "To determine risk factors for coronavirus disease (COVID-19) among US healthcare personnel (HCP), we conducted a case–control analysis. We collected data about activities outside the workplace and COVID-19 patient care activities from HCP with positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) test results (cases) and from HCP with negative test results (controls) in healthcare facilities in 5 US states. We used conditional logistic regression to calculate adjusted matched odds ratios and 95% CIs for exposures. Among 345 cases and 622 controls, factors associated with risk were having close contact with persons with COVID-19 outside the workplace, having close contact with COVID-19 patients in the workplace, and assisting COVID-19 patients with activities of daily

> living. Protecting HCP from COVID-19 may require interventions that reduce their exposures outside the workplace and improve their ability to more safely assist COVID-19 patients with activities of daily living."

Mental Health and Wellness

News in Brief

"The pandemic has caused nearly two years of collective trauma. Many people are near a breaking point" (WP).

"When facing loss, embrace change and don't force closure, a therapist urges" (NPR).

Journal Articles

MMWR Surveill Summ: Suicidal Thoughts and Behaviors Among Adults Aged ≥18 Years — United States, 2015–2019 (07 January 2022)

> "Problem/Condition: Suicidal thoughts and behaviors are important public health concerns in the United States. In 2019, suicide was the 10th leading cause of death among persons aged ≥18 years (adults); in that year, 45,861 adults died as a result of suicide, and an estimated 381,295 adults visited hospital emergency departments for nonfatal, self-inflicted injuries. Regional- and state-level data on self-inflicted injuries are needed to help localities establish priorities and evaluate the effectiveness of suicide prevention strategies.
>
> Period Covered: 2015–2019.
>
> Description of System: The National Survey on Drug Use and Health (NSDUH) is an annual survey of a representative sample of the civilian, noninstitutionalized U.S. population aged ≥12 years. NSDUH collects data on the use of illicit drugs, alcohol, and tobacco; initiation of substance use; substance use disorders and treatment; health care; and mental health. This report summarizes data on responses to questions concerning suicidal thoughts and behaviors contained in the mental health section among sampled persons aged ≥18 years in all 50 states and the District of Columbia. This report summarizes 2015–2019 NSDUH data collected from 254,767 respondents regarding national-, regional-, and state-level prevalence of suicidal thoughts, planning, and attempts by age group, sex, race and ethnicity, region, state, education, marital status, poverty level, and health insurance status.
>
> Results: Prevalence estimates of suicidal thoughts and behaviors varied by sociodemographic factors, region, and state. During 2015–2019, an estimated 10.6 million

> (annual average) adults in the United States (4.3% of the adult population) reported having had suicidal thoughts during the preceding year. The prevalence of having had suicidal thoughts ranged from 4.0% in the Northeast and South to 4.8% in the West and from 3.3% in New Jersey to 6.9% in Utah. An estimated 3.1 million adults (1.3% of the adult population) had made a suicide plan in the past year. The prevalence of having made suicide plans ranged from 1.0% in the Northeast to 1.4% in the Midwest and West and from 0.8% in Connecticut and New Jersey to 2.4% in Alaska. An estimated 1.4 million adults (0.6% of the adult population) had made a suicide attempt in the past year. The prevalence of suicide attempts ranged from 0.5% in the Northeast to 0.6% in the Midwest, South, and West and from 0.3% in Connecticut to 0.9% in West Virginia. Past-year prevalence of suicidal thoughts, suicide planning, and suicide attempts was higher among females than among males, higher among adults aged 18–39 years than among those aged ≥40 years, higher among noncollege graduates than college graduates, and higher among adults who had never been married than among those who were married, separated, divorced, or widowed. Prevalence was also higher among those living in poverty than among those with a family income at or above the federal poverty threshold and higher among those covered by Medicaid or the Children’s Health Insurance Program than among those with other types of health insurance or no health insurance coverage.
>
> Interpretation: The findings in this report highlight differences in the adult prevalence of suicidal thoughts, plans to attempt suicide, and attempted suicide during the 12 months preceding the survey at the national, regional, and state levels during 2015–2019. Geographic differences in suicidal thoughts and behavior varied by sociodemographic characteristics and might be attributable to sociodemographic composition of the population, selective migration, or the local cultural milieu. These findings underscore the importance of ongoing surveillance to collect locally relevant data on which to base prevention and intervention strategies.
>
> Public Health Action: Understanding the patterns of and risk factors for suicide is essential for designing, implementing, and evaluating public health programs for suicide prevention and policies that reduce morbidity and mortality related to suicidal thoughts and behaviors. State health departments and federal agencies can use the results from this report to assess progress toward achieving national and state health objectives in suicide prevention. Strategies might include identifying and supporting persons at risk, promoting connectedness, and creating protective environments."

Ann Behav Med: [Psychological Predictors of Self-reported COVID-19 Outcomes: Results From a Prospective Cohort Study]() (03 January 2022)

> "Background: Previous research has shown that psychological factors, such as stress and social support, are associated with greater susceptibility to viral respiratory illnesses and more severe symptoms. During the COVID-19 pandemic there has been a well-documented

> deterioration in psychological well-being and increased social isolation. This raises questions as to whether those experiencing psychological adversity during the pandemic are more at risk of contracting and/or experiencing COVID-19 symptoms.
>
> Purpose: To examine the relationship between psychological factors and the risk of COVID-19 self-reported infection and the symptomatic experience of SARS-CoV-2 (indicated by the number and severity of symptoms).
>
> Methods: As part of a longitudinal prospective observational cohort study, 1,087 adults completed validated measures of psychological well-being during April 2020 and self-reported incidence of COVID-19 infection and symptom experience across the pandemic through to December 2020. Regression models were used to explore these relationships controlling for demographic and occupational factors.
>
> Results: Greater psychological distress during the early phase of the pandemic was significantly associated with subsequent self-reported SARS-CoV-2 infection as well as the experience of a greater number and more severe symptoms.
>
> Conclusions: COVID-19 infection and symptoms may be more common among those experiencing elevated psychological distress. Further research to elucidate the mechanisms underlying these associations is needed."

Psychiatry Res Commun: Early psychological health outcomes among United States healthcare professionals, essential workers, and the general population during the COVID-19 pandemic: The influence of occupational status (01 November 2021)

> "The primary purpose of this study was to determine variations in psychological experiences of the COVID-19 pandemic among US healthcare workers, non-healthcare essential workers, and the general population. A cross-sectional survey was conducted online from June 22, 2020 to July 5, 2020, with 5,023 participants aged 18 years and older. The prevalence of fear of COVID-19 and symptoms of depression, anxiety, and posttraumatic stress disorder were evaluated, using the Fear of COVID-19 Scale, Patient Health Questionnaire-8, Generalized Anxiety Disorder-7, and Posttraumatic Diagnostic Scale. Generalized linear mixed-effects models were used to explore sociodemographic and COVID-19-related risk factors. Using models unadjusted for working status, it was found healthcare workers endorsed less fear of COVID-19, depression, and PTSD symptoms, than the general public. After adjusting for working status, no further significant differences were found between occupational groups. Across all psychological distress outcomes, those who were not working or were unemployed due to COVID-19 reported more symptoms than did individuals who continued to work from their normal location or remotely. A similar trend was found for nurses and physicians, with members of both groups reporting symptoms of depression, anxiety, and PTSD less when working from their normal location than when unemployed due to COVID-19."

Disparities and Health Equity

News in Brief

"Vaccine gap between Black and White Americans narrowed, but it's back for booster shots" (WP).

Opinion: "Recognizing obesity as a disease, not a choice, is a step toward health equity" (STAT).

Long Reads

"The lost girls of Covid: The pandemic is erasing decades of progress in young women's health, education, and independence in developing nations" (Bloomberg).

"How medicine erased Black women from a 'white man's disease'" (STAT).

Journal Articles

JAMA Netw Open: Assessment of Regional Variability in COVID-19 Outcomes Among Patients With Cancer in the United States (04 January 2022)

> "Question: To what extent are spatiotemporal trends in the COVID-19 pandemic in the United States associated with outcomes for patients with cancer infected with SARS-CoV-2?
>
> Findings: This cohort study of 4749 patients with cancer and COVID-19 found no significant differences in outcomes across the 9 US census divisions. Overall, outcomes significantly improved between March and December 2020, and treatment at cancer centers in less densely populated counties was associated with better outcomes.
>
> Meaning: These findings suggest that understanding the heterogeneity in COVID-19 outcomes between cancer centers could guide resource allocation and help the oncology community improve COVID-19 outcomes for this patient population."

JAMA Health Forum: Variation in Use of Surgical Care During the COVID-19 Pandemic by Surgical Urgency and Race and Ethnicity (23 December 2021)

> "Question: To what extent did the COVID-19 pandemic reduce access to surgical care, and were racial and ethnic minority groups more likely to have reduced access to surgical care?
>
> Findings: In this cohort study of more than 13 million inpatient and outpatient surgical encounters in 767 US hospitals in a hospital administrative database, surgical use was 13% lower in 2020 compared with 2019, with the greatest decrease concentrated in elective surgical procedures. While Black and Hispanic patients experienced a reduction in surgical encounters, White patients experienced the greatest reduction in surgical encounters.

> Meaning: Despite severe and persistent disruptions to health systems during the COVID-19 pandemic, racial and ethnic minority groups did not experience a disproportionate decrease in access to surgical care."

Transmission, Exposure, and Testing

News in Brief

"How do I know if I have a cold, the flu or COVID-19?" (AP)

Testing

"SARS-CoV-2 viral mutations: impact on COVID-19 tests" (FDA).

"Scientists try to pinpoint why rapid Covid tests are missing some cases" (STAT).

"At-home covid tests and omicron: What you need to know" (WP).

"Study raises doubts about rapid Covid tests' reliability in early days after infection" (STAT; see also: medRxiv preprint).

Long Reads

"Here's why rapid COVID tests are so expensive and hard to find" (ProPublica).

Journal Articles

Clin Infect Dis: Quantifying environmental mitigation of aerosol viral load in a controlled chamber with participants diagnosed with COVID-19 (06 January 2022)

> "Background: Several studies indicate that COVID-19 is primarily transmitted within indoor spaces. Therefore, environmental characterization of SARS-CoV-2 viral load with respect to human activity, building parameters, and environmental mitigation strategies is critical to combat disease transmission.
>
> Methods: We recruited 11 participants diagnosed with COVID-19 to individually occupy a controlled chamber and conduct specified physical activities under a range of environmental conditions; we collected human and environmental samples over a period of three days for each participant.
>
> Results: Here we show that increased viral load, measured by lower RNA cycle threshold (CT) values, in nasal samples is associated with higher viral loads in environmental aerosols and on surfaces captured in both the near field (1.2 m) and far field (3.5 m). We also found

> that aerosol viral load in far field is correlated with the number of particles within the range of 1 µm -2.5 µm. Furthermore, we found that increased ventilation and filtration significantly reduced aerosol and surface viral loads, while higher relative humidity resulted in lower aerosol and higher surface viral load, consistent with an increased rate of particle deposition at higher relative humidity. Data from near field aerosol trials with high expiratory activities suggest that respiratory particles of smaller sizes (0.3 µm -1 µm) best characterize the variance of near field aerosol viral load.
>
> Conclusions: Our findings indicate that building operation practices such as ventilation, filtration, and humidification substantially reduce the environmental aerosol viral load, and therefore inhalation dose, and should be prioritized to improve building health and safety."

Emerg Infect Dis: Airborne Transmission of SARS-CoV-2 Delta Variant within Tightly Monitored Isolation Facility, New Zealand (Aotearoa) (29 December 2021)

> "In New Zealand, international arrivals are quarantined and undergo severe acute respiratory syndrome coronavirus 2 screening; those who test positive are transferred to a managed isolation facility (MIF). Solo traveler A and person E from a 5-person travel group (BCDEF) tested positive. After transfer to the MIF, person A and group BCDEF occupied rooms >2 meters apart across a corridor. Persons B, C, and D subsequently tested positive; viral sequences matched A and were distinct from E. The MIF was the only shared location of persons A and B, C, and D, and they had no direct contact. Security camera footage revealed 4 brief episodes of simultaneous door opening during person A’s infectious period. This public health investigation demonstrates transmission from A to B, C, and D while in the MIF, with airborne transmission the most plausible explanation. These findings are of global importance for coronavirus disease public health interventions and infection control practices."

Clin Infect Dis: Predictors of SARS-CoV-2 infection following high-risk exposure (21 December 2021)

> "Background: Non-pharmaceutical interventions (NPIs) are recommended for COVID-19 prevention. However, the effectiveness of NPIs in preventing SARS-CoV-2 transmission remains poorly quantified.
>
> Methods: We conducted a test-negative design case-control study enrolling cases (testing positive for SARS-CoV-2) and controls (testing negative) with molecular SARS-CoV-2 diagnostic test results reported to California Department of Public Health between 24 February-12 November, 2021. We used conditional logistic regression to estimate adjusted odds ratios (aORs) of case status among participants who reported contact with an individual known or suspected to have been infected with SARS-CoV-2 ("high-risk exposure") ≤14 days before testing.

> Results: 751 of 1448 cases (52%) and 255 of 1443 controls (18%) reported high-risk exposures ≤14 days before testing. Adjusted odds of case status were 3.02-fold (95% confidence interval: 1.75-5.22) higher when high-risk exposures occurred with household members (vs. other contacts), 2.10-fold (1.05-4.21) higher when exposures occurred indoors (vs. outdoors only), and 2.15-fold (1.27-3.67) higher when exposures lasted ≥3 hours (vs. shorter durations) among unvaccinated and partially-vaccinated individuals; excess risk associated with such exposures was mitigated among fully-vaccinated individuals. Cases were less likely than controls to report mask usage during high-risk exposures (aOR=0.50 [0.29-0.85]). The adjusted odds of case status was lower for fully-vaccinated (aOR=0.25 [0.15-0.43]) participants compared to unvaccinated participants. Benefits of mask usage were greatest among unvaccinated and partially-vaccinated participants, and in interactions involving non-household contacts or interactions occurring without physical contact.
>
> Conclusions: NPIs reduced the likelihood of SARS-CoV-2 infection following high-risk exposure. Vaccine effectiveness was substantial for partially and fully vaccinated persons."

Other Infectious Diseases and Public Health Threats

News in Brief

"5 years later, researchers assess how children exposed to Zika are developing" (NPR).

"3 fatal rabies cases in U.S. suggest public underestimates infection risks" (STAT; see also: MMWR Notes from the Field).

"Military families say they were ill months before jet-fuel leak brought scrutiny to Pearl Harbor's tap water" (WP).

Journal Articles

Clin Infect Dis: Mortality for adults entering HIV care under universal early treatment compared to the general US population (04 January 2022)

> "Background: Mortality among adults with HIV remains elevated over mortality in the US general population even in the years after entry into HIV care. We explore whether the elevation in 5-year mortality would have persisted if all adults with HIV had initiated antiretroviral therapy within 3 months of entering care.

> Methods: Among 82,766 adults entering HIV care at North American AIDS Cohort Collaboration clinical sites in the United States, we computed mortality over 5 years since entry into HIV care under observed treatment patterns. We then used inverse probability weights to estimate mortality under universal early treatment. To compare mortality with similar individuals in the general population, we used National Center for Health Statistics data to construct a cohort representing the subset of the US population matched to study participants on key characteristics.
>
> Results: For the entire study period (1999 - 2017), 5-year mortality among adults with HIV was 7.9 percentage points (95% confidence interval (CI): 7.6, 8.2) higher than the expected mortality based on the US general population. Under universal early treatment, the elevation in mortality for people with HIV would have been 7.2% (95% CI: 5.8, 8.6). In the most recent calendar period examined (2011-2017), the elevation in mortality for people with HIV was 2.6 percentage points (95% CI: 2.0, 3.3) under observed treatment patterns and 2.1 percentage points (95% CI: 0.0, 4.2) under universal early treatment.
>
> Conclusions: Expanding early treatment may modestly reduce, but not eliminate, the elevation in mortality for people with HIV."

Clin Infect Dis: Human papillomavirus antibody levels following vaccination or natural infection among young men who have sex with men (31 December 2021)

> "Background: Australia introduced a school-based gender-neutral human papillomavirus (HPV) vaccination program for schoolgirls and boys aged 12-13 years in 2013. We examined HPV type specific antibody levels in unvaccinated young men who have sex with men (MSM) with natural infection and compared these to levels in those vaccinated against HPV.
>
> Methods: Serum specimens at baseline were collected from MSM aged 16-20 years in the HYPER1 and HYPER2 studies, conducted between 2010-2013 and 2017-2019, respectively. Merck's 4-plex HPV competitive Luminex Immunoassay was used to quantify HPV6, 11, 16 and 18 specific antibodies. We compared antibody levels for each HPV genotype between unvaccinated men (HYPER1) and vaccinated men (HYPER2) using the Mann-Whitney U test.
>
> Results: There were 200 unvaccinated men and 127 vaccinated men included in the analysis. Median antibody levels among vaccinated men were significantly higher than levels among unvaccinated men for HPV6 (223 mMU/ml vs 48 mMU/ml, p<0.0001), HPV11 (163 mMU/ml vs 21 mMU/ml, p<0.0001), HPV16 (888 mMU/ml vs 72 mMU/ml, p<0.0001) and HPV18 (161 mMU/ml vs 20 mMU/ml, p<0.0001). The median time between antibody level measurement and last vaccine dose was 47.7 (IQR 40.4 to 54.1) months. Antibody levels did not change over time for up to 66 months for all four genotypes among vaccinated men.

> Conclusion: Among young MSM vaccinated with the quadrivalent HPV vaccine, antibody levels for HPV 6, 11, 16 and 18 were significantly higher than those in unvaccinated MSM following natural infection. Antibody levels following vaccination appeared to remain stable over time."

Lancet Glob Health: Impact of the SARS-CoV-2 pandemic on routine immunisation services: evidence of disruption and recovery from 170 countries and territories (21 December 2021)

> "Background: The SARS-CoV-2 pandemic has revealed the vulnerability of immunisation systems worldwide, although the scale of these disruptions has not been described at a global level. This study aims to assess the impact of COVID-19 on routine immunisation using triangulated data from global, country-based, and individual-reported sources obtained during the pandemic period.
>
> Methods: This report synthesised data from 170 countries and territories. Data sources included administered vaccine-dose data from January to December, 2019, and January to December, 2020, WHO regional office reports, and a WHO-led pulse survey administered in April, 2020, and June, 2020. Results were expressed as frequencies and proportions of respondents or reporting countries. Data on vaccine doses administered were weighted by the population of surviving infants per country.
>
> Findings: A decline in the number of administered doses of diphtheria-pertussis-tetanus-containing vaccine (DTP3) and first dose of measles-containing vaccine (MCV1) in the first half of 2020 was noted. The lowest number of vaccine doses administered was observed in April, 2020, when 33% fewer DTP3 doses were administered globally, ranging from 9% in the WHO African region to 57% in the South-East Asia region. Recovery of vaccinations began by June, 2020, and continued into late 2020. WHO regional offices reported substantial disruption to routine vaccination sessions in April, 2020, related to interrupted vaccination demand and supply, including reduced availability of the health workforce. Pulse survey analysis revealed that 45 (69%) of 65 countries showed disruption in outreach services compared with 27 (44%) of 62 countries with disrupted fixed-post immunisation services.
>
> Interpretation: The marked magnitude and global scale of immunisation disruption evokes the dangers of vaccine-preventable disease outbreaks in the future. Trends indicating partial resumption of services highlight the urgent need for ongoing assessment of recovery, catch-up vaccination strategy implementation for vulnerable populations, and ensuring vaccine coverage equity and health system resilience."

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Statistics

	Total Cases	*Total Deaths*	*Total Vaccine Doses Administered*
Global	300,559,516	5,474,526	9,366,203,731
United States	58,489,268	833,996	Not available

JHU CSSE as of 1000 EDT 07 January 2022

Virginia	Total cases (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	1,221,036	36,815	19,601	26,065	30,934	16,100	13,867	65,529
Hospitalizations	44,056	1,412	853	881	1,684	1,017	830	3,087
Deaths	15,651	382	257	320	370	256	258	605

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